

<b>Interview Summary</b>	<b>Application No.</b> 10/786,400	<b>Applicant(s)</b> OXFORD ET AL.	
	<b>Examiner</b> Tamthom N. Truong	<b>Art Unit</b> 1624	

All participants (applicant, applicant's representative, PTO personnel):

(1) Tamthom N. Truong.

(3) Colleen McKiernan.

(2) Christine O'Day.

(4) \_\_\_\_\_.

Date of Interview: 05 July 2007.

Type: a) ☒ Telephonic b) ☐ Video Conference  
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☐ Yes e) ☐ No.

If Yes, brief description: \_\_\_\_\_.

Claim(s) discussed: 53 and 59.

Identification of prior art discussed: N/A.

Agreement with respect to the claims f) ☐ was reached. g) ☐ was not reached. h) ☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: For claim 53, the examiner advised Ms. O'Day to limit the diseases to asthma and COPD or provide compelling evidences for all recited diseases. The examiner also suggested Ms. O'Day to delete "cystic fibrosis" from claim 53, and cancel claim 59 since it depends on claim 43 which has been cancelled.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.



Examiner's signature, if required

7/15/07 - Christine O'Day  
2- Colleen McKiernan

Docket No.: 56476DIV2(300610)  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Alexander W. Oxford et al.

Application No.: 10/786,400

Confirmation No.: 2879

Filed: February 24, 2004

Art Unit: 1624

For: DERIVATIVES OF PYRIMIDO [6,1-a]  
ISOQUINOLIN-4-ONE

Examiner: T. N. Truong

**FOR DISCUSSION ONLY- DO NO ENTER**

Examiner Truong  
Via Facsimile only  
671-273-0676  
9 Pages

Dear Examiner Truong:

**INTRODUCTORY COMMENTS**

Thank you for your careful consideration and allowance of the indicated claims.

Further to your discussion with Christine O'Day earlier today, please consider the following claims for the purpose of discussion only. Please do not enter the claims below into the formal record.

Claims 1-42 and 49-50 stand canceled. Claims 44, 45, and 60-63 are allowed. Claims 53, and 55 have been amended. Claims 43, 54 and 56-57 have been canceled. To facilitate review of the claims, the allowed claims have been noted in the claim identifiers.

Please contact Colleen McKiernan at 617-517-5555 (cmckiernan@eapdlaw.com) if you have any problems with the facsimile.

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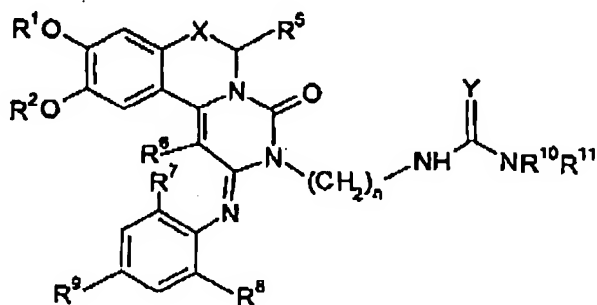
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**AMENDMENTS TO THE CLAIMS**

Claims 1-42 (cancelled).

Claim 43 (cancelled):

Claim 44 (previously presented- allowed): A method for the treatment of asthma in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of formula I:



I

wherein

each of R<sup>1</sup> and R<sup>2</sup> independently represents a C<sub>1-6</sub> alkyl or C<sub>2-7</sub> acyl group;

R<sup>5</sup> represents a hydrogen atom or a C<sub>1-3</sub> alkyl, C<sub>2-3</sub> alkenyl or C<sub>2-3</sub> alkynyl group;

R<sup>6</sup> represents a hydrogen atom or a C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, amino, C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub>) alkylamino or C<sub>2-7</sub> acylamino group;

each of R<sup>7</sup> and R<sup>8</sup> independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy,

C<sub>3-6</sub> cycloalkyl; and

R<sup>9</sup> represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy or C<sub>3-6</sub> cycloalkyl group;

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X represents a group  $CR^3R^4$ , wherein each of  $R^3$  and  $R^4$  independently represents a hydrogen atom or a  $C_{1-3}$  alkyl group;

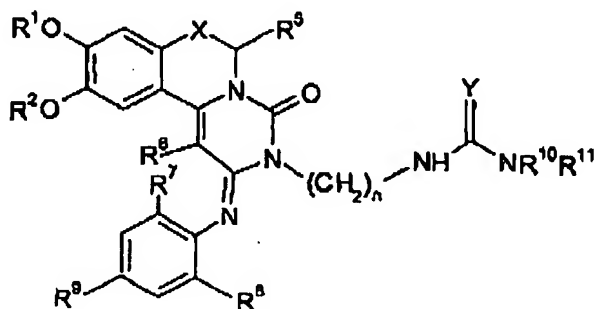
each of  $R^{10}$  and  $R^{11}$  independently represents a hydrogen atom, a  $C_{1-3}$  alkyl,  $C_{3-6}$  cycloalkyl or phenyl group;

Y represents an oxygen atom or a group  $CHNO_2$ ,  $NCN$ ,  $NH$  or  $NNO_2$ ;

n is an integer from 2 to 4;

or a salt thereof.

Claim 45 (previously presented- allowed): A method for the treatment of chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of formula I:



I

wherein

each of  $R^1$  and  $R^2$  independently represents a  $C_{1-6}$  alkyl or  $C_{2-7}$  acyl group;

$R^5$  represents a hydrogen atom or a  $C_{1-3}$  alkyl,  $C_{2-3}$  alkenyl or  $C_{2-3}$  alkynyl group;

$R^6$  represents a hydrogen atom or a  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, amino,  $C_{1-6}$  alkylamino,  $di(C_{1-6})$  alkylamino or  $C_{2-7}$  acylamino group;

each of  $R^7$  and  $R^8$  independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy,

$C_{3-6}$  cycloalkyl; and

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$R^9$  represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy or  $C_{3-6}$  cycloalkyl group;

X represents a group  $CR^3R^4$ , wherein each of  $R^3$  and  $R^4$  independently represents a hydrogen atom or a  $C_{1-3}$  alkyl group;

each of  $R^{10}$  and  $R^{11}$  independently represents a hydrogen atom, a  $C_{1-3}$  alkyl,  $C_{3-6}$  cycloalkyl or phenyl group;

Y represents an oxygen atom or a group  $CHNO_2$ ,  $NCN$ ,  $NH$  or  $NNO_2$ ;

n is an integer from 2 to 4;

or a salt thereof.

Claim 46 (previously presented): A method as claimed in any one of claims 43, 44 or 45, wherein independently or in any compatible combination:

each of  $R^1$  and  $R^2$  independently represent a  $C_{1-6}$  alkyl;

each of  $R^3$  and  $R^4$  represents a hydrogen atom;

$R^5$  represents a hydrogen atom;

$R^6$  represents a hydrogen atom;

each of  $R^7$  and  $R^8$  independently represent a  $C_{1-6}$  alkyl;

$R^9$  represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group  $CHNO_2$ ; and

n is 2.

Claim 47 (previously presented): A method as claimed in any one of claims 43 to 45, wherein the compound is administered by aerosol.

Claim 48 (previously presented): A method as claimed in any one of claims 43 to 45, wherein the mammal is a human.

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Claims 49-50 (cancelled).

Claim 51 (previously presented): A method as claimed in any one of claims 43 to 45, wherein each of R<sup>1</sup> and R<sup>2</sup> represents a C<sub>1-4</sub> alkyl group; and each of R<sup>7</sup> and R<sup>8</sup> represents a methyl, ethyl or isopropyl group.

Claim 52 (previously presented): A method as claimed in any one of claims 43 to 45, wherein the compound of general formula I is selected from the group consisting of:

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(*N*-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-isopropylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-methyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-isopropyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*, *N'*-dimethyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-phenylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-2-one;

9,10-Dimethoxy-3-[2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-3-[*N*-(*N'*-nitro)-2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-[*N*-(*N'*-Cyclohexylcarbamoyl)-2-aminoethyl]-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-(*N*-Carbamoyl-2-aminoethyl)-9,10-dimethoxy-2-(2-methylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

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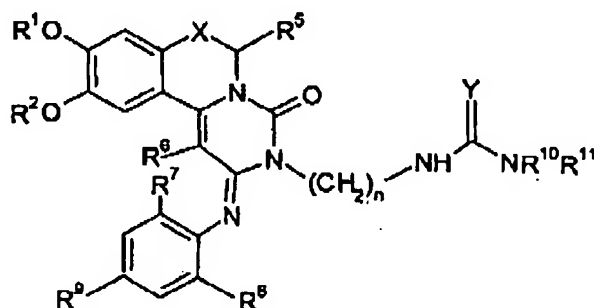
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3-(*N*-Carbamoyl-2-aminoethyl)-2-(2,6-diisopropylphenylimino)-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-(*N*-Carbamoyl-4-aminobutyl)-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one; and

3-[*N*-(*N'*-Cyano-*N''*-methyl)-2-guanidinoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one.

(Claim 53 (previously presented): A method of treating a disease in a mammal in need of a smooth muscle relaxant and/or an anti-inflammatory compound, comprising administering to a subject an effective, non-toxic amount of a compound of formula I:



I

wherein

each of  $R^1$  and  $R^2$  independently represents a  $C_{1-6}$  alkyl or  $C_{2-7}$  acyl group;

$R^5$  represents a hydrogen atom or a  $C_{1-3}$  alkyl,  $C_{2-3}$  alkenyl or  $C_{2-3}$  alkynyl group;

$R^6$  represents a hydrogen atom or a  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, amino,  $C_{1-6}$  alkylamino, di( $C_{1-6}$ ) alkylamino or  $C_{2-7}$  acylamino group;

each of  $R^7$  and  $R^8$  independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy,

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C<sub>3-6</sub> cycloalkyl; and

R<sup>9</sup> represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>2-7</sub> acyl, C<sub>1-6</sub> alkylthio, C<sub>1-6</sub> alkoxy or C<sub>3-6</sub> cycloalkyl group;

X represents a group CR<sup>3</sup>R<sup>4</sup>, wherein each of R<sup>3</sup> and R<sup>4</sup> independently represents a hydrogen atom or a C<sub>1-3</sub> alkyl group;

each of R<sup>10</sup> and R<sup>11</sup> independently represents a hydrogen atom, a C<sub>1-3</sub> alkyl, C<sub>3-6</sub> cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO<sub>2</sub>, NCN, NH or NNO<sub>2</sub>;

n is an integer from 2 to 4;

or a salt thereof, wherein the disease is a respiratory disorder is selected from the group consisting of asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), and cystic fibrosis.

Claim 54 (canceled):

Claim 55 (currently amended): The method of claim 54 55, wherein the respiratory disorder is selected from the group consisting of asthma, ~~allergic asthma~~, hay fever, and allergic rhinitis, ~~bronchitis~~, ~~chronic obstructive pulmonary disease (COPD)~~, ~~adult respiratory distress syndrome (ARDS)~~, and ~~cystic fibrosis~~.

Claim 56 (canceled):

Claim 57 (canceled):

Claim 58 (previously presented): The method of claim 43, wherein the disease is characterized by an increased eosinophil count in lung of the mammal.



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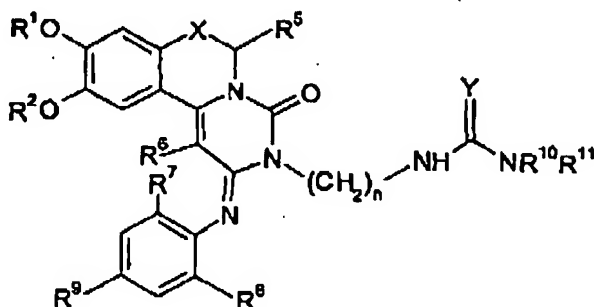
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Claim 59 (previously presented): The method of claim 43, wherein the phosphodiesterase inhibitor is a phosphodiesterase type III inhibitor or a phosphodiesterase type IV inhibitor.

*is cancelled*  
*should cancel*

*is it clear?*

Claim 60 (previously presented- allowed): A method to treat asthma or to cause bronchial dilation in a mammal in need thereof, comprising administering to said mammal an effective, non-toxic amount of a compound of formula I:



I

wherein

each of  $R^1$  and  $R^2$  independently represents a  $C_{1-6}$  alkyl or  $C_{2-7}$  acyl group;

$R^5$  represents a hydrogen atom or a  $C_{1-3}$  alkyl,  $C_{2-3}$  alkenyl or  $C_{2-3}$  alkynyl group;

$R^6$  represents a hydrogen atom or a  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl, amino,  $C_{1-6}$  alkylamino, di( $C_{1-6}$ ) alkylamino or  $C_{2-7}$  acylamino group;

each of  $R^7$  and  $R^8$  independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy,

$C_{3-8}$  cycloalkyl; and

$R^9$  represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl,  $C_{1-6}$  alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $C_{2-7}$  acyl,  $C_{1-6}$  alkylthio,  $C_{1-6}$  alkoxy or  $C_{3-8}$  cycloalkyl group;

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X represents a group  $\text{CR}^3\text{R}^4$ , wherein each of  $\text{R}^3$  and  $\text{R}^4$  independently represents a hydrogen atom or a  $\text{C}_{1-3}$  alkyl group;

each of  $\text{R}^{10}$  and  $\text{R}^{11}$  independently represents a hydrogen atom, a  $\text{C}_{1-3}$  alkyl,  $\text{C}_{3-6}$  cycloalkyl or phenyl group;

Y represents an oxygen atom or a group  $\text{CHNO}_2$ ,  $\text{NCN}$ ,  $\text{NH}$  or  $\text{NNO}_2$ ;

n is an integer from 2 to 4;

or a salt thereof.

Claim 61 (previously presented- allowed): The method of claim 60, wherein independently or in any compatible combination;

each of  $\text{R}^1$  and  $\text{R}^2$  independently represent a  $\text{C}_{1-6}$  alkyl;

each of  $\text{R}^3$  and  $\text{R}^4$  represents a hydrogen atom;

$\text{R}^5$  represents a hydrogen atom;

$\text{R}^6$  represents a hydrogen atom;

each of  $\text{R}^7$  and  $\text{R}^8$  independently represent a  $\text{C}_{1-6}$  alkyl;

$\text{R}^9$  represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group  $\text{CHNO}_2$ ; and

n is 2.

Claim 62 (previously presented- allowed): The method of claim 60, wherein the compound is administered by aerosol.

Claim 63 (previously presented- allowed): The method of claim 60, wherein the mammal is a human.